REMARKS

Claims 1, 2, 4-23, 28-54 and 67-72 are pending in the instant application. Claims 4-6, 13, 28-48, 51-54 and 68-72 have been withdrawn from consideration. Claims 1, 2, 7-12, 14-23, 49, 50 and 67 have been rejected. Claims 4-6, 13, 28-48, 51-54 and 68-72 have been canceled. Claims 1 and 50 have been amended. No new matter has been added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Election/Restriction

The Restriction Requirement wherein Applicants have elected SEQ ID NO: 78, human interleukin-5, has been deemed proper and made Final. Accordingly, claims 4-6, 13, 28-48, 51-54 and 68-72 have been canceled, with Applicants reserving the right to file continuing applications on the canceled subject matter.

II. Rejection of Claims Under 35 U.S.C. 112, First Paragraph

The rejection of claim 50 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art

to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, has been maintained. The Examiner suggests that the specification as filed does not enable *in vivo* uses of the claimed antisense compounds, including treatment of human asthma. Applicants respectfully disagree with this rejection of claim 50.

At the outset, Applicants respectfully point out that claim 50 is directed to a method of modulating the expression of interleukin-5 in cells or tissues. Nowhere does this claim state that the method is a method of treating human asthma as suggested by the Examiner. The specification as filed presents data showing both *in vitro* (see pages 49-59 and 67-71 of the specification as filed) and *in vivo* (see pages 60-64 of the specification as filed) modulation of interleukin-5 expression in cells or tissues of animals. For example, experiments were performed and presented in the specification as filed demonstrating that the antisense compounds of the instant invention were effective when given to animals *in vivo*. In one set of experiments, eosinophilia was prevented in mice dosed *in vivo* with antisense oligonucleotides. In another set of experiments, IL-5 levels were shown to be decreased in mice *in vivo* after pre-treatment with antisense

compounds of the instant invention. In a third set of experiments, an art-accepted mouse model for human allergic asthma, the antisense compounds of the instant invention were shown to have therapeutic activity. Therefore, contrary to the Examiner's opinion, the specification as filed demonstrates that the compounds of the instant invention are pharmacologically active *in vivo* to reduce IL-5 levels, the method that is now claimed. Nowhere does the claim as amended recite a method of treatment or a method of disease prevention; it instead is a method for modulating interleukin-5 levels in cells and tissues. Accordingly, withdrawal of this rejection is respectfully requested.

III. Rejection of Claims Under 35 U.S.C. 103(a)

The rejection of claims 1, 2, 7-12, 14-23, 49 and 50 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Weltman et al., and further in view of Dolgonov et al., Sahasrabudhe et al. (1996), Baracchini et al. (US Patent 5,801,154), and Fritz et al. (1997) has been maintained for reasons of record. The Examiner suggests it would have been *prima facie* obvious for one of ordinary skill to combine the teachings of Weltman et al., Dolgonov et al., Baracchini et al., and Fritz et al. to make the instant invention

because Weltman teaches antisense to IL-5 and use of antisense to inhibit gene expression, Dolgonov teach an antisense compound with 100% homology to a sequence claimed, Baracchini et al. disclose modification of antisense as claimed as well as target regions of antisense compounds as claimed, and Fritz et al. teach use of drug delivery systems as claimed for oligonucleotides. The Examiner suggests that motivation is provided by the teachings of Baracchini, Weltman and Dolgonov, while Baracchini, Fritz, and Sahasrabudhe provide motivation for modification of oligonucleotides as claimed. Applicants respectfully traverse this rejection.

At the outset, Applicants have amended the claims to list specific nucleobase regions within the sequence of human interleukin-5 (SEQ ID NO: 78) that are to be targeted by antisense compounds. These nucleobase regions are taught in the specification as filed at pages 64-72.

Weltman et al. (US Patent 6,048,726) disclose a single 16 mer antisense oligonucleotide that has the ability to inhibit expression of IL-5 *in vitro*. The antisense compound was designed to be antisense to an area within the coding region of human IL-5. No other targets for antisense within the sequence of human IL-5 are

taught by this reference. In addition, only one particular sequence for a coding region targeted antisense compound is taught. Nowhere does this patent teach regions of IL-5 other than the coding region of human IL-5 that might be targeted specifically with antisense. Further, this patent fails to teach any of the specific nucleobase regions as now claimed.

The secondary references cited fail to overcome the deficiencies in teaching of this primary reference.

As discussed in the previous response dated November 14, 2002, Dolgonov et al. fail to teach a specific sequence of the instant invention as claimed by the Examiner. Therefore, this patent fails to teach or suggest the object of the instant invention as claimed and adds no teaching to support a case of *prima facie* obviousness.

Sahasrabudhe et al. (1996) disclose the effects of stereoisomerism at the point of attachment of a peptide to an oligonucleotide, as a conjugate. Nowhere does this patent teach or suggest antisense compounds targeted to specific nucleobase regions of an interleukin-5 nucleic acid molecule as now claimed.

The '154 patent teaches modification to antisense oligonucleotides in general as a way to enhance activity and also general large target regions within the sequence of a gene other

than interleukin-5 of SEQ ID NO: 78. However, this general discussion of modified oligonucleotides and general target regions does not teach or suggest use of antisense compounds of any type to target specific nucleobase regions of the interleukin-5 nucleic acid molecule as now claimed, and the successful inhibition of expression using antisense.

Fritz et al. (1997) disclose and characterize model drug carrier systems for antisense oligonucleotides. However, nowhere does this paper teach or suggest antisense compounds targeted to specific nucleobase regions of a human interleukin-5 nucleic acid molecules as now claimed.

To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP 2143. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all claim limitations. The limitations of the claims as now amended, which recite specific nucleobase regions within the sequence of human interleukin-5 of SEQ ID NO: 78, are not taught or suggested by any of the references

individually or when combined. It is only with the specification in hand that one of skill would know which nucleobase regions to target with antisense compounds. Therefore, the limitations of the claims as amended clearly are not taught or suggested by the combination of prior art references, nor is any expectation of successful use of such region targeted antisense compounds provided by the combination of prior art. Thus, the combination of prior art cited cannot render the instant claimed invention obvious. Withdrawal of this rejection is therefore respectfully requested.

IV. Double Patenting

Claims 1, 2, 7, 8, 14-23, 49, 50 and 67 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 5-15, 26, 27 and 30 of US Patent No. 6,136,603. The Examiner suggests that although the conflicting claims are not identical they are not patentably distinct from each other. Applicants are filing herewith a terminal disclaimer as required under 37 CFR 1.130. Accordingly, withdrawal of this rejection is respectfully requested.

V. Rejection of Claims Under 35 U.S.C. 112, Second Paragraph

Claim 50 has been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants have amended claim 50 to correct the antecedent basis. Withdrawal of this rejection is respectfully requested.

VI. Objection to Claim 1

Claim 1 and its dependent claims have been objected to as being drawn to non-elected subject matter. Claim 1 has been amended to correct this situation. Withdrawal of this objection is respectfully requested.

VII. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly,

favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

Jane Massey Licata
Registration No. 32,257

Date: July 17, 2003

Licata & Tyrrell P.C.
66 E. Main Street
Marlton, NJ 08053

856-810-1515